IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH, Plaintiff, v. IMPAX LABORATORIES, INC., Defendant.	Civil Action No.: 06-222 JJF **PUBLIC VERSION**

DEFENDANT IMPAX LABORATORIES, INC.'S
OPENING CLAIM CONSTRUCTION BRIEF

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Original Dated: May 8, 2007
Public Version: May 15, 2007

TABLE OF CONTENTS

Page(s)

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES
(cont.)

Page(s)

Other Authorities

I. INTRODUCTION

This case arises under the Hatch-Waxman Act, which was promulgated in large part to reduce the exorbitant price of prescription drugs by speeding the introduction of generic substitutes. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990); *Andrx Pharm., Inc, v. Biovail Corp. Int'l*, 256 F.3d 799, 809 (D.C. Cir. 2001) ("Congress sought to get generic drugs into the hands of patients at reasonable prices—fast"). This litigation represents an effort by Wyeth to subvert the purpose of that Act in two ways. First, Wyeth has already litigated and lost most of the claim construction issues it is pressing here; Wyeth is now forum shopping among district courts in an effort to delay the ultimate resolution of these issues. Second, by seeking to exclude virtually any extended-release formulation of venlafaxine from the market, Wyeth is trying to extend its monopoly on venlafaxine beyond its legitimate term.

Wyeth holds a patent on venlafaxine, an anti-depressant. Since 1994, Wyeth has made billions of dollars in sales of venlafaxine under the brand name Effexor. Wyeth's patent on venlafaxine does not expire until 2008. Impax has not challenged Wyeth's patent on venlafaxine, and has not sought FDA approval to market an extended release version of venlafaxine until after Wyeth's patent on venlafaxine expires.

Concerned that its monopoly on venlafaxine was coming to end, however, Wyeth developed an "extended release" formulation of the drug that could be taken once a day rather than two or three times a day. Wyeth named this product Effexor XR. Wyeth now seeks to construe the claims of its patents broadly to cover virtually any extended release version of venlafaxine, notwithstanding its repeated representations in the patent specification that its "invention" was a specific extended release formulation.[1]

This ploy has already proven unsuccessful. Wyeth originally brought suit in the District of New Jersey against Teva Pharmaceuticals when Teva announced its intent to sell a generic version of extended release venlafaxine. Wyeth made essentially the same claim construction

[1] A chart setting forth the parties' respective constructions of the disputed claims is attached as Exhibit A to the accompanying Declaration of Mary B. Matterer (hereafter "Ex.").

arguments that it is advancing here. The New Jersey court rejected those arguments and held that the claims of Wyeth's patents were properly construed as congruent with what Wyeth had actually invented—an extended release formulation comprised of certain ingredients as set forth in the patent specification. Teva's extended release formulation (like Impax's extended release formulation) is different from Wyeth's extended release formulation. As a result, Wyeth could have stipulated to a judgment of non-infringement and argued its claim construction position to the Federal Circuit. Instead, however, Wyeth settled its case with Teva, setting up its current strategy to take a second shot at a broader claim construction in this Court – and in three other district courts around the United States.[2]

The opinion of the New Jersey court was detailed and well reasoned. There is no reason for this Court to reach a different conclusion.

II. BACKGROUND

A. Wyeth's Development of Venlafaxine

In 1983, Wyeth filed for a patent on the compound now known as venlafaxine.[3] The specification of that patent identified the compound's utility as an antidepressant.[4] The patent issued on August 13, 1985, and will expire on December 13, 2007.[5]

B. Wyeth's Development of Extended Release Venlafaxine

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[2] *See Wyeth v. Osmotica Pharm. Corp.*, No. 7:07-cv-00067 (E.D.N.C. filed Apr. 20, 2007); *Wyeth v. Lupin Ltd.*, No. 1:07-cv-00632 (D. Md. filed March 12, 2007); *Wyeth v. Anchen Pharms.*, No. 8:06-cv-386 (C.D. Cal. filed April 12, 2006).

[3] Ex. C (U.S. Patent No. 6,274,171, "Extended release formulation of venlafaxine hydrochloride") at column 4, lines 9-12 (hereafter "4:9-12") ("The extended release formulations of this invention are comprised of 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol hydrochloride in admixture with [MCC] and [HPMC]."); Ex. D (U.S. Patent No. 4,535,186) (filed Oct. 26, 1983) at 24:18-20 (claiming the compound 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol and salts thereof).

[4] Ex. C ('186 Patent) (cover page).

[5] *Id*; Ex. E (certificate of term extension of the '186 Patent).

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Wyeth initially tried to develop a venlafaxine tablet using hydrogel technology, but discovered that the tablet dissolved too quickly *in vitro*: "Numerous attempts to produce extended release tablets by hydrogel technology proved to be fruitless because the compressed tablets were either physically unstable (poor compressibility or capping problems) or dissolved too rapidly in dissolution studies."[8] Wyeth pursued that avenue no further, concluding that development of such a venlafaxine tablet using hydrogel technology was "impossible."[9]

Nor was this Wyeth's only failure: the patents describe a series of "failed experiments"[10] in making spheroids using an extrusion and spheronization process.[11] The specification contends that it was "completely unexpected that an extended release formulation containing venlafaxine hydrochloride could be obtained because the hydrochloride of venlafaxine proved to be extremely water soluble."[12] Wyeth tested and rejected certain ingredients because they did not yield the desired results.[13] Ultimately, Wyeth identified specific ingredients—microcrystalline cellulose (hereafter "MCC") and optionally hydroxypropylmethylcellulose (hereafter "HPMC")—which could be used to make venlafaxine spheroids by extrusion and spheronization.[14] The specification contains no teaching regarding how to avoid replicating Wyeth's failed experiments other than by making the specific formulations of the invention,

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8 *Id.* at 4:60-64.

9 *Id.* at 10:53-55.

10 *Id.* at 6:6.

11 *Id.* at 5:1-11; *see* Declaration of Arthur H. Kibbe ("Kibbe Decl.") ¶ 30 (explaining the extrusion and spheronization process).

12 Ex. C at 4:57-60.

13 *Id.*

14 *Id.* at 5:11-13.

comprising venlafaxine, MCC, and, optionally, HPMC.[15]

C. The Patents in Suit and their Prosecution History

There are three patents at issue in this case: U.S. Patent Nos. 6,274,171, 6,419,958, and 6,403,120. The three patents share an identical specification.

The Abstracts of the patents provide that "**the invention** comprises an extended release formulation of venlafaxine hydrochloride in spheroids comprised of venlafaxine hydrochloride, [MCC] and, optionally, [HPMC] coated with a mixture of ethyl cellulose and [HPMC]."[16] The Brief Description of the Invention similarly recites that "**[t]he formulations of this invention** comprise an extended release formulation of venlafaxine hydrochloride comprising a therapeutically effective amount of venlafaxine hydrochloride in spheroids comprised of venlafaxine hydrochloride, [MCC] and, optionally, [HPMC] coated with a mixture of ethyl cellulose and [HPMC]."[17] The Detailed Description of the Invention further describes "**the extended release formulations of this invention**" as comprised of venlafaxine hydrochloride "in admixture with [MCC] and [HPMC]."[18]

After this discussion of the "formulations of this invention," the specification then describes various "preferred embodiment[s] of this invention," each of which is comprised of the previously recited ingredients in varying proportions.[19] The specification provides seven examples "to illustrate applicant's solution to the problem of the preparation of the extended release drug containing formulations of this invention."[20] Each of the examples is comprised of venlafaxine hydrochloride, MCC and, optionally, HPMC.[21] The Detailed Description states that

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[15] Kibbe Decl. ¶¶ 15-18.

[16] Ex. C at Abstract (emphasis added).

[17] *Id.* at 2:63-3:2 (emphasis added).

[18] *Id.* at 4:9-12 (emphasis added).

[19] *Id.* at 3:17-62.

[20] *Id.* at 5:29-31.

[21] *Id.* at 5:33-10:57.

the preferred embodiment uses Avicel® PH101 brand MCC and Dow® K3 brand HPMC.[22] The specification notes that other brands of those ingredients may be substituted "without changing the inventive concept"[23] but nowhere describes using any ingredients other than those described as comprising "the invention."[24] The specification concludes that "the desired dissolution rates of sustained release dosage forms of venlafaxine hydrochloride, impossible to achieve using hydrogel tablet technology, has been achieved with the film-coated spheroid compositions of this invention."[25]

In the first (non-provisional) application in the chain that led to the issuance of the patents in suit, Wyeth initially proposed formulation claims that were explicitly limited to formulations of venlafaxine hydrochloride, MCC, and HPMC.[26] Wyeth also proposed method claims similar to those at issue here, which did not explicitly recite the ingredients of the formulation to be administered using the claimed method.[27]

The examiner found the method claims invalid over a prior art patent which explicitly disclosed administering venlafaxine in a "sustained oral administration form or time-release form, which may be used to spread the doseage [sic] over time, such as for once-a-day applications."[28] The examiner insisted that Wyeth make explicit that its method claims were limited to the formulations described in the specification.[29] Wyeth agreed to amend the method claims to make them depend from the narrow formulation claims and obtained a Notice of

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[22] *Id.* at 4:26-33.

[23] *Id.* at 4:44-47.

[24] *Id.* at Abstract.

[25] *Id.* at 10:53-57.

[26] Ex. G (excerpt from file history of U.S. Patent App. No. 08/821,137) at 11. The optional nature of HPMC first appeared in U.S. Patent App. No. 08/964,328. *See* Ex. L (excerpt from file history of U.S. Patent App. No. 08/964,328) at 12.

[27] *Id.* at 12.

[28] Ex. I (U.S. Patent No. 5,506,270) at 5:25-27; Ex. H (finding the claims invalid in light of the '270 patent).

[29] Ex. H.

Allowance.[30] However, rather than allowing those claims to issue, Wyeth then abandoned that application and filed a new application which was assigned to a different examiner.[31] Wyeth then re-proposed method claims virtually identical to the original (unamended) claims from the earlier application.[32] Wyeth did not tell the new examiner about the prior application, nor that a different examiner had rejected virtually identical claims and that Wyeth had agreed to amend these claims in order to overcome the prior art. After another abandonment and re-filing, the new examiner allowed the method claims to issue.[33]

D. Others succeeded where Wyeth had failed

Wyeth tried and failed to make a formulation of venlafaxine that would release slowly over time using hydrogel tablet technology. However, another company, Synthon, was able to make such a tablet, accomplishing what Wyeth had deemed "impossible."[34] Impax's formulation likewise does not derive from the teachings of the patents in suit.

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In the patented invention, a spheroid containing venlafaxine, MCC, and, optionally, HPMC is created using a process known as "extrusion and spheronization."[35] MCC is particularly suited to the "extrusion and spheronization" process.[36] Indeed, a 1984 study showed

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[30] *Id.*

[31] Ex. J (abandoning the '137 Application, which was assigned to Examiner Hulina); Ex. K (excerpt from file history of U.S. Patent App. No. 08/964,328) (indicating assignment of the '328 Application to Examiner Spear).

[32] Ex. L at 14 (excerpt from file history of U.S. Patent App. No. 08/964,328).

[33] Ex. C (cover page) (listing Examiner Spear as the Primary Examiner); *Id.* at 12:63-13:12 (setting forth method claims identical to those rejected by Examiner Hulina in the '137 Application).

[34] Ex. M (U.S. Patent No. 6,696,496) (describing a hydrogel tablet dosage form of Venlafaxine).

[35] Ex. C at 1:38-47; Kibbe Decl. ¶ 30 (describing the "extrusion and spheronization" process); HANDBOOK OF PHARMACEUTICAL GRANULATION TECHNOLOGY 336-52 (2d ed. 2005) (Ex. N) (same).

[36] Kibbe Decl. ¶ 31.

that the extrusion and spheronization process is impossible using any common pharmaceutical excipient other than MCC.[37] The spheroids are then coated with a controlled-release coating.[38]

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III. LEGAL ARGUMENT

A. The Legal Principles of Claim Construction

A claim term can be given its correct construction only within the context of "what the inventors actually invented and intended to envelop with the claim." *Phillips v. AWH Corp.*, 415 F.3d at 1303, 1316 (Fed. Cir. 2005). A claim term should be construed to mean "what one of ordinary skill in the art at the time of the invention would have understood the term to mean." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 986 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). But "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the

[37] HANDBOOK OF PHARMACEUTICAL GRANULATION TECHNOLOGY 352 (2d ed. 2005) (Ex. N) (reporting results of a 1984 study by O'Connor et al.).

[38] Ex. C at 1:46-47

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entire patent, including the specification." *Phillips*, 415 F.3d at 1313. "In general, the scope and outer boundary of claims is set by the patentee's description of his invention." *On Demand Mach. Corp. v. Ingram Indus., Inc.*, 442 F.3d 1331, 1338 (Fed. Cir. 2006). The specification is usually "dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Moreover, a patentee is free to serve as his own lexicographer: "if the patent inventor clearly supplies a different meaning [from the ordinary meaning], the claim should be interpreted accordingly." *Adobe Sys. Inc. v. Macromedia, Inc.*, 201 F. Supp. 2d 309, 314 (D. Del. 2002) (citing *Markman*, 52 F.3d at 980).

A court may consult extrinsic evidence, such as dictionaries, expert and inventor testimony, but extrinsic evidence is "less significant" and "less reliable" than intrinsic evidence because it gives meaning to a claim term in the abstract, rather than in the particular context of the patent. *Phillips*, 415 F.3d at 1317-18. Thus, extrinsic sources of evidence may play a supporting role in claim construction, "as long as those sources are not used to contradict claim meaning that is unambiguous in light of the intrinsic evidence." *Id.* at 1324. If possible, claims should be construed to uphold their validity. *In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984).

B. An Extended Release Formulation is defined in the specification to include MCC and optionally HPMC

Disputed Term	Impax's Construction	Wyeth's Construction
extended release formulation	a formulation comprising venlafaxine, microcrystalline cellulose, and, optionally, HPMC coated with a mixture of ethyl cellulose and HPMC in an amount needed to provide a specific unit dosage administered once-a-day to provide a therapeutic blood plasma level of venlafaxine over the entire 24-hour period of administration	A formulation, other than a hydrogel tablet, which releases the active ingredient at a slower rate than the immediate release formulation of the active ingredient such that the dosing frequency is once-a-day rather than the plural daily dosing for the immediate release formulation.

1. The *Teva* court correctly concluded that the inventors defined extended release formulation to include MCC and, optionally, HPMC

This Court does not need to reinvent the wheel in construing the term "extended release formulation." The New Jersey court considered the same claim construction issue that is presented here, analyzed Wyeth's arguments carefully, and issued a 21-page opinion rejecting them. *See* Ex. B (*Markman* opinion in *Wyeth v. Teva Pharms.*, No. 03-CV-1293 (D.N.J. Sep. 6, 2005), *vacated after settlement*) (hereafter "*Teva*"). Had Wyeth been convinced that the New Jersey court got it wrong, Wyeth could have stipulated to a judgment of non-infringement and appealed the *Teva* court's claim construction to the Federal Circuit. Instead, Wyeth settled with Teva, and then filed a new case against Impax in a different forum—much as Wyeth acquiesced in the first examiner's rejection of Wyeth's method claims, abandoned its application, filed a continuation, and then tried to gain allowance of the same rejected claims from a different examiner. In this circumstance, it is appropriate for this Court to afford substantial deference, if not outright preclusive effect, to the New Jersey court's decision. *See, e.g., KX Indus., L.P. v. PUR Water Purification Prods., Inc.*, 108 F. Supp. 2d 380, 387 (D. Del. 2000), *aff'd*, 18 Fed. Appx. 871 (Fed. Cir. 2001) (deferring to a prior claim construction "to the extent the parties do not raise new arguments"); *Texas Instruments, Inc. v. Linear Techs. Corp.*, 182 F. Supp. 2d 580 (E.D. Tex. 2002) (court may defer to a prior claim construction, though not necessarily bound by it); *Abbott Labs. v. Dey, L.P.*, 110 F. Supp. 2d 667 (N.D. Ill. 2000) (applying issue preclusion to a claim construction by another district court, although also considering whether the previous construction was "plainly wrong"); *TM Patents, L.P. v. IBM Corp.*, 72 F. Supp. 2d 370 (S.D.N.Y. 1999) (ruling that prior claim construction by a different district court was entitled to preclusive effect).

In the prior litigation against Teva, Wyeth argued that the term "extended release formulation" meant "[a] formulation which releases the active ingredient at a slower rate than the immediate release formulation of the active ingredient such that the dosing frequency is once-a-day rather than the plural daily dosing for the immediate release formulation." *Teva* at 6. Teva

advanced precisely the same argument that we make here: the patentees expressly defined the term "extended release formulation" in the specification to mean "[a] formulation comprising venlafaxine hydrochloride, [MCC] and, optionally, [HPMC] coated with a mixture of ethyl cellulose and [HPMC] in an amount needed to provide a specific unit dosage administered once-a-day to provide a therapeutic blood plasma level of venlafaxine over the entire 24-hour period of administration." *Id.* (emphasis omitted).

The *Teva* court concluded that "[w]hen the term 'extended release formulation' is looked at in its proper context in the specification, this Court believes that one of ordinary skill in the art would construe the term to include specific ingredients." *Id.* at 11. The court explained that "[a]lthough it is improper to limit claim terms based on nothing more than the disclosed embodiments," limitations defined by the inventors in the specification are controlling, and here the inventors had specifically defined the meaning of "extended release formulation" in the specification. *Id.* at 9-10.

2. The claims are properly construed to be no broader than what the inventors invented.

There can be no doubt that the inventors defined "the invention" to be a formulation comprised of specific ingredients. This is not merely a case in which a particular formulation is described as being a preferred embodiment of the invention. Nor is it even merely a case in which all the preferred embodiments comprise a particular formulation. Instead, this is a case in which the inventors repeatedly described their "invention" as being a particular formulation. The inventors repeatedly refer to "the formulations of this invention" and "the extended release formulations of this invention" as comprising venlafaxine hydrochloride, MCC and, optionally, HPMC.[44] "Although claims need not be limited to the preferred embodiment when the invention is more broadly described, 'neither do the claims enlarge what is patented beyond what the inventor has described as the invention.'" *Inpro II Licensing, S.A.R.L. v. T-Mobile USA, Inc.*, 450 F.3d 1350, 1355 (Fed. Cir. 2006) (quoting *Network, LLC v. Centraal Corp.*, 242 F.3d 1347,

[44] Ex. C at 2:63-3:2, 4:9-12.

1352 (Fed. Cir. 2001)).

The Federal Circuit's recent decision in *Honeywell International, Inc. v. ITT Industries, Inc.*, 452 F.3d 1312 (Fed. Cir. 2006) is particularly instructive. There, the district court construed a "fuel injection system component" to mean "a fuel filter," notwithstanding that the ordinary meaning of a fuel injection system component "refers to any constituent part of the fuel injection system of a motor vehicle including, for example, fuel filters, fuel lines, and connectors." *Honeywell*, 452 F.3d at 1315-16. Indeed, the applicants had made statements in the prosecution history suggesting that the term "fuel injection system component" was broader than only fuel filters. *Id.* at 1316. However, in the written description, "the 'invention' was identified to be only a fuel filter." *Id.* Thus, "[g]iven the written description, the [district] court concluded that the patentee characterized a fuel filter as the only embodiment of his invention, not merely a preferred version of all possible embodiments." *Id.* (internal quotation omitted). The Federal Circuit affirmed, analyzing the issue in terms that apply precisely to this case:

> Here, the written description uses language that leads us to the conclusion that a fuel filter is the only 'fuel injection system component' that the claims cover, and that a fuel filter was not merely discussed as a preferred embodiment. On at least four occasions, the written description refers to the fuel filter as 'this invention' or 'the present invention' . . . . **The public is entitled to take the patentee at his word and the word was that the invention is a fuel filter.**

Id. at 1318. Here, just as in *Honeywell*, the public (and Impax) is entitled to take Wyeth at its word, and Wyeth's word was that the invention is a formulation with specific ingredients.

In other cases, the Federal Circuit has similarly construed claims to be no broader than the invention disclosed in the patent. For example, in *SciMed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337,1338 (Fed. Cir. 2001), the claims recited a catheter. Two types of catheters were known in the art: dual and coaxial. *SciMed*, 242 F.3d at 1339. The Federal Circuit concluded that the term catheter should be construed as limited to a coaxial catheter because "the characterization of the coaxial configuration as part of the 'present invention' is strong evidence that the claims should not be read to encompass the opposite structure." *Id.* at 1343. *See also Watts v. XL Sys., Inc.*, 232 F.3d 877, 883 (Fed. Cir. 2000)

(noting that the specification states that "the present invention" used the feature at issue); *Alloc, Inc. v. ITC*, 342 F.3d 1361, 1368-69 (Fed. Cir. 2003) (relying on the patent specification's description of "the invention"); *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1348 (Fed. Cir. 2004) (construing claims to be consistent with "Summary of the Invention").

In *Astrazeneca AB v. Mutual Pharmaceutical. Co.*, 384 F.3d 1333, 1339-40 (Fed. Cir. 2004), the court construed "solubilizer" to mean a particular kind of solubilizer (a "surfactant") because the specification recited that "the solubilizers suitable according to the invention are defined below" as limited to surfactants. The court reasoned that the use of the definite article "the"—as in "**the** solubilizers according to the invention" or "**the** extended release formulation of this invention"—is strong evidence that the inventors were setting forth definitions and not merely examples. *Id.* Moreover, the Federal Circuit has repeatedly held that an inventor need not use any explicit definitional format, but instead can define a term by implication. *See Bell Atl. Network Servs. v. Covad Commc'ns Group, Inc.*, 262 F.3d 1258, 1271 (Fed. Cir. 2001) ("[W]hen a patentee uses a claim term throughout the entire patent specification, in a manner consistent with only a single meaning, he has defined that term by implication.") (internal quotation omitted).

The inventors' description of their invention as limited to a formulation comprising MCC and optionally HPMC was no accident: it embraced what the inventors actually invented, but not more. The inventors could have said that their invention merely "included" a particular formulation, were that true. The specification contains no such broadening language. Indeed, the very choice of the word "formulation" implies that the invention has specific ingredients. The everyday meaning of "formulation" implies specific ingredients: a "formulation" is "the product of formulating;" "formulating" is "reduc[ing] to express[ing] in or as if in a formula;" a "formula" is "a recipe or prescription giving method and proportions of ingredients for the preparation of some material (as a medicine, a blend of coffee, or a caulking compound)." WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 894 (2002) (Ex. O).

The inventors repeatedly described their invention in terms that would make no sense if they claimed to have invented *any* extended release venlafaxine formulation. The specification's repeated reference to the "optional[]" inclusion of HPMC shows that the other ingredients – venlafaxine hydrochloride and MCC – are not optional.[45] Moreover, the inventors' explicit recitation that other brands of HPMC could be substituted makes clear the limited nature of the substitutions that the inventors believed to be possible within the scope of the invention. There would have been no reason for the inventors to explain that other brands of HPMC "having the same chemical and physical characteristics as the proprietary products named above may be substituted in the formulation without changing the inventive concept" if the "inventive concept" were not limited to a particular set of ingredients.[46]

It is therefore hardly surprising that every example in the specification conforms to the inventors' definition of their invention, and comprises venlafaxine hydrochloride, MCC and, optionally, HPMC.[47] While the fact that all embodiments set forth in a patent specification share a common element does not by itself mandate that the claims be construed to include that element, the similarity of all the embodiments further supports a narrow construction. *See, e.g., Wang Labs, Inc. v. Am. Online, Inc.*, 197 F.3d 1377, 1383 (Fed. Cir. 1999); *Netword, LLC v. Centraal Corp.*, 242 F.3d 1347, 1352 (Fed. Cir. 2001).

A person of ordinary skill in the art would understand that the inventors had only developed formulations that contained venlafaxine hydrochloride, MCC and, optionally, HPMC, coated with a mixture of ethyl cellulose and HPMC in an amount needed to provide a specific unit dosage administered once-a-day to provide a therapeutic blood plasma level of venlafaxine over the entire 24-hour period of administration.[48] No other successful formulations are disclosed, discussed, or suggested by the specification. At the time of the patent filing,

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[45] *See* Ex. C at Abstract & 2:63-3:2; Kibbe Decl. ¶ 14.

[46] Ex. C at 4:44-47.

[47] *Id.* at 5:33-10:57.

[48] Kibbe Decl. ¶¶ 10-14.

numerous other extended release technologies—drug-coated sugar beads, diffusion systems, reservoir systems, enteric coatings and wax coatings—were known and understood in the art.[49] A person having ordinary skill in the art would know of all these extended release technologies, because they are taught in basic classes and textbooks, and had been used for many years with a wide variety of active ingredients.[50] Many of these known extended release technologies work in a completely different way than the Wyeth formulation disclosed in the specification. Such technologies can use different ingredients performing different functions, perform the functions in different ways, and differ in their results.[51] The patent contains no teaching regarding how to make an extended release formulation of venlafaxine using any of these different ingredients.

3. Wyeth's proposed construction is litigation-driven construction-by-hindsight

In the *Teva* case, Wyeth repeatedly scolded Teva for changing its claim construction positions during the course of the litigation.[52] Then, Wyeth argued that "extended release formulation" carried its ordinary meaning. *Teva* at 6. But now Wyeth has changed its tune, and argues that the term "extended release formulation" does not simply carry its ordinary meaning, as Wyeth previously contended, but instead means "[a] formulation, **other than a hydrogel tablet,** which releases the active ingredient at a slower rate than the immediate release formulation of the active ingredient such that the dosing frequency is once-a-day rather than the plural daily dosing for the immediate release formulation." Wyeth's new construction fares no better than its old one. In the *Teva* case, Wyeth at least could argue that its proposed definition was consistent with the ordinary meaning of "extended release formulation." Now Wyeth must concede that "extended release formulation" does not bear its ordinary meaning; thus, the court must look to the specification to define the term. But the specification does not suggest that the inventors intended to exclude *only* hydrogel tablets from the scope of their invention. Hydrogel

[49] *Id.* ¶ 19.

[50] *Id.*

[51] *Id.* ¶ 20.

[52] Ex. P (excerpt from Wyeth's opening claim construction brief in the *Teva* case).

tablets were only one of a succession of failed experiments.[53]

Wyeth will presumably argue here, as it did before, that if the term "extended release formulation" is construed to mean the extended release formulations that are described in the specification, some of the claims of the '120 patent would have the same scope. That is true, but it is not dispositive, and the *Teva* court correctly rejected that argument as unpersuasive. The doctrine of claim differentiation is only a guide; it is "not a hard and fast rule of construction." *Comark Commc'ns., Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998); *see Multiform Dessicants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1480 (Fed. Cir. 1998) ("[T]he doctrine of claim differentiation can not broaden claims beyond their correct scope, determined in light of the specification and the prosecution history and any relevant extrinsic evidence."). Here, "the unequivocal language the patentees used when describing their invention—'the invention comprises an extended release formulation of', 'the formulations of this invention comprise' and 'the extended release formulations of this invention are'—rebuts the presumption established by the doctrine of claim differentiation." *Teva* at 11 (citing *Kraft Foods, Inc. v. Int'l Trading Co.*, 203 F.3d 1362, 1368-69 (Fed. Cir. 2000)).

Wyeth also likely will complain that Impax's proposed construction leads to redundancy within the language of the claims themselves. This is likewise true, and likewise not dispositive, as the *Teva* court also held. *Teva* at 6-7, 12. Indeed, there is redundancy in the claim language even under Wyeth's proposed construction. For example, claim 21 of the '171 patent claims "a method for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride, which comprises administering ... an ... extended release formulation..., said formulation containing venlafaxine hydrochloride as the active ingredient."[54] Because the claim requires "the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride," venlafaxine hydrochloride is necessarily the active ingredient, and thus the final limitation is superfluous,

[53] Kibbe Decl. ¶¶ 15-18.

[54] Ex. C at 13:4-12.

even under Wyeth's construction.

4. The prosecution history bars Wyeth's attempt to claim formulations other than those described in the specification.

The Federal Circuit has held that a patentee cannot acquiesce in an examiner's rejection of its claims and then later seek to recapture that same claim scope without explicitly telling the examiner about the need to revisit the prior art upon which the earlier rejection had been based. In *Hakim v. Cannon Avent Group, PLC*, 479 F.3d 1313, 1315-16 (Fed. Cir. 2007), the patentee initially submitted claims to a drinking cup with a "slit" and distinguished over the prior art on the basis that the prior art did not disclose a slit. The examiner allowed the claims. *Id.* at 1316. The patentee then filed a continuation application accompanied by a letter explaining that he had made a broadening amendment to the claims, changing the term "slit" to "opening." *Id.* The continuation claims were allowed without comment or rejection by the examiner. *Id.* The Federal Circuit held that the term "opening" was properly construed to mean a "slit." *Id.* at 1318. "Although a disclaimer made during prosecution can be rescinded, permitting recapture of disclaimed claim scope, the prosecution history must be sufficiently clear to inform the examiner that the previous disclaimer, and the prior art that it was made to avoid, may need to be revisited." *Id.*

The facts here present an even more compelling case for a narrow claim construction than did *Hakim*. In *Hakim*, the applicant had at least informed the examiner by letter that he was making a broadening amendment, and the same examiner reviewed both the original and the amended claims. Here, however, a first examiner rejected claims that did not explicitly recite the composition of the extended release formulation and required that the claims be made dependent from the formulation claims (which did). *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 33 (1997) ("the court should presume that the PTO had a substantial reason related to patentability for including the limiting element added by amendment"). Wyeth agreed during the Examiner Interview to narrow the claims, thereby acquiescing in the examiner's rejection. Without submitting a response to the Notice of Allowance, Wyeth then abandoned that

application and resubmitted the same claims before a different examiner without noting either the fact of the prior rejection or the prior art upon which the rejection had been based. Under *Hakim*, Wyeth is precluded from arguing that an "extended release formulation" does not include MCC and, optionally, HPMC, consistent with the first examiner's refusal to allow broader claims.

C. "Incidence" of nausea and emesis refers to the number of patients with nausea and emesis

Disputed Term	Impax's Construction	Wyeth's Construction
with diminished incidence(s) of nausea and emesis	a decrease in the number of patients suffering from nausea and vomiting compared to patients receiving the same total daily dose of an immediate release formulation that is administered at least twice a day	The degree and/or frequency of nausea and emesis from the extended release formulation administered once-a-day is less than what would be experienced by patients receiving the same total daily dose of an immediate release formulation that is administered at least twice a day.

The New Jersey court's order from the *Teva* litigation resolves not only the meaning of "extended release formulation," but the meaning of "incidence" as well. Some of the asserted claims require that the extended release formulation of the invention result in a "diminished incidence(s) of nausea and emesis."[55] The parties' claim construction positions are identical to those that were advanced by Wyeth and Teva in the earlier litigation. Now, as then, the parties agree that the term "incidence" includes the frequency of an event, such that the incidence of nausea and emesis refers to the frequency of nausea and emesis within the patient population. And, now as then, the parties disagree as to whether "incidence" also includes the "level" or severity of those side effects.

A person of ordinary skill in the art at the time the patent applications were filed would understand that "level" and "incidence" are two distinct terms of art.[56] Incidence refers to the number of patients who experience an event.[57] Level refers to the severity or intensity of an

[55] *E.g.*, Ex. C at 12:65.

[56] Declaration of Bertram A. Spilker ("Spilker Decl.") ¶ 13.

[57] *Id.*

event.[58] Medical dictionaries confirm this definition of "incidence." *Id.* ¶ 16; *see, e.g.*, BASIC & CLINICAL BIOSTATISTICS 407 (4th ed. 2004) ("**incidence** A rate giving the proportion of people who develop a given disease or condition within a specified period of time.") (Spilker Decl. Exhibit 3); ILLUSTRATED DICTIONARY AND RESOURCE DIRECTORY OF ENVIRONMENTAL & OCCUPATIONAL HEALTH 331 (2d Ed. 2005) ("incidence – (*epidemiology*) The number of cases of disease, infection, or some other event having an onset during a prescribed period of time in relation to the unit of population in which they occur.") (Spilker Decl. Exhibit 5). The specification explicitly distinguishes between incidence and level. It explains that "this invention reduces by adaptation, the level of nausea and the incidence of emesis that attend the administration of multiple daily dosing."[59] The use of these two distinct terms in the specification "must be because the patentees meant to differentiate between these two terms." *Teva* at 18.

The specification further explains that "with the plural daily dosing regimen, the most common side effect is nausea, experienced by about forty five percent of patients under treatment with venlafaxine hydrochloride."[60] The New Jersey court correctly concluded that this "passage makes clear that the patentees were concerned with the number of patients experiencing side effects, not necessarily the severity of those side effects." *Teva* at 17. The Abstract also notes that the invention "provides a lower incidence of nausea and vomiting than the conventional tablets."[61] From this, the New Jersey court concluded that "[b]ecause the only discussion of the conventional tablets in the specification that is relevant to the term incidence concerns the percent of patients that experienced side effects, the abstract supports a narrow construction." *Teva* at 17.

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[58] *Id.*

[59] Ex. C at 2:47-49.

[60] Ex. C at 2:7-11.

[61] Ex. C at Abstract.

Wyeth likely will argue that the specification would support claims directed to reducing the level of nausea, not merely the incidence of nausea. But as the *Teva* court also explained, "'[t]he fact that a patent asserts that an invention achieves several objectives does not require that each of the claims be construed as limited to structures that are capable of achieving all of the objectives.'" *Teva* at 18 (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 908 (Fed. Cir. 2004)). Wyeth could have attempted to claim a reduction in the level of nausea; it did not do so. It is not this Court's task to rewrite the claims, but merely to determine what the claims as written mean. *See Chef America, Inc. v. Lamb-Weston, Inc.*, 358 F.3d 1371 (Fed. Cir. 2004). Here, the claims are directed to the incidence of nausea and emesis, not the level of nausea and emesis, and should be so construed.

D. Wyeth's proposed definition of "troughs and peaks" reads in limitations that are not present in the claims.

Disputed Term	Impax's Construction	Wyeth's Construction
[A method] for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride	the peak(s) and trough(s) due to the "therapeutic metabolism" of any second or third dose given in a single day is eliminated by dosing only once every 24 hours	A method in which the extended release formulation is administered once in a 24-hour period, resulting in a venlafaxine blood plasma concentration that rises to a maximum value, followed by a generally protracted decrease over the remaining period while maintaining during that 24-hour period levels of venlafaxine in blood plasma that are sufficient to provide, during the course of treatment, relief from the condition being treated, thereby eliminating the multiple sharp peaks and troughs resulting from multiple daily dosing of the same total daily dose of the immediate release formulation as reflected in a graph of venlafaxine blood plasma concentration versus time.

1. The term "therapeutic metabolism" has no meaning to a person of ordinary skill in the art.

Every patent specification must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112. Claims that are "not amenable to construction" or "insolubly ambiguous" are indefinite. *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005). "[I]f reasonable efforts at claim construction prove futile," a claim term should be deemed indefinite. *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). Claims are *required* to be "sufficiently precise" so that a potential competitor may "determine whether or not he is infringing . . . ." *Morton Int'l v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993). Where a claim fails this test, it is "invalid for failure to satisfy the 'definiteness' requirement of section 112, second paragraph." *Id.*

The term "therapeutic metabolism of plural daily doses" simply has no meaning to a person of skill in the art.[62] While "therapeutic" and "metabolism" each have meanings, the combination of the two words is not commonly used by persons of skill in the art, and thus has no ordinary meaning.[63] Nor does the context of the claim or specification clarify what is meant by "therapeutic metabolism of plural daily doses." Indeed, the specification of the patents cannot provide an answer, because it does not even use the term "therapeutic metabolism."

2. Wyeth's proposed construction imports additional limitations into the claim.

Wyeth's proposed construction has a number of other defects. Wyeth proposes a long, drawn out definition that impermissibly imports into the claim language many additional limitations.[64] The preamble to Claim 24 is representative: "A method for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride."[65] Generally speaking, there are two peaks

[62] Spilker Decl. ¶ 18; Kibbe Decl. ¶ 29.

[63] *Id.*

[64] *See* Ex. A.

[65] Ex. C at 14:5-8.

and two troughs in a patient's blood plasma concentration when a drug is given twice a day, but a drug that is given once a day would only have one peak and one trough. *Id.* A person of ordinary skill in the art would understand this to mean that the trough(s) and peak(s) resulting from plural daily doses are eliminated by dosing only once per day.[66]

Wyeth's construction takes this relatively simply concept of once-a-day dosing and converts it into a complicated graph. Specifically, Wyeth proposes:

> A method in which the extended release formulation is administered once in a 24-hour period, resulting in a venlafaxine blood plasma concentration that rises to a maximum value, followed by a generally protracted decrease over the remaining period while maintaining during that 24-hour period levels of venlafaxine in blood plasma that are sufficient to provide, during the course of treatment, relief from the condition being treated, thereby eliminating the multiple sharp peaks and troughs resulting from multiple daily dosing of the same total daily dose of the immediate release formulation as reflected in a graph of venlafaxine blood plasma concentration versus time.[67]

Wyeth's construction adds no fewer then 9 limitations to the claim:

1) a venlafaxine blood plasma concentration that rises to a maximum value
2) followed by a generally protracted decrease
3) over the remaining period
4) while maintaining during that 24-hour period levels of venlafaxine in blood plasma that are sufficient to provide,
5) during the course of treatment,
6) relief from the condition being treated,
7) thereby eliminating the multiple sharp peaks and troughs
8) resulting from multiple daily dosing of the same total daily dose of the immediate release formulation
9) as reflected in a graph of venlafaxine blood plasma concentration over time.

Wyeth's proposed construction seems literally to require a graph to determine whether one

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[66] Spilker Decl. ¶ 19.

[67] *See* Ex. A.

infringes the claim.

Contrary to Wyeth's proposed construction, the preamble does not provide any insight as to the specific shape of a graph of the drug concentration in a patient's blood plasma, other than that it eliminates the trough(s) and peak(s). The preamble language does not tell a person of ordinary skill in the art the slope or shape of the blood plasma curve over time, the magnitude of that curve, whether the magnitude of the troughs or peaks change with respect to the once a day or plural daily doses, or whether the trough(s) or peak(s) are sharp or more moderate.[68] Nor is there anything about providing unspecified relief during an unspecified "course of treatment."

In contrast, Impax's proposed construction simply states that "the peak(s) and trough(s) due to the 'therapeutic metabolism' of any second or third dose given in a single day is eliminated by dosing only once every 24 hours." This construction comports with the plain meaning of the terms.

IV. CONCLUSION

Impax respectfully requests that the Court adopt the following constructions:

"extended release formulation" - a formulation comprising venlafaxine, MCC, and, optionally, HPMC coated with a mixture of ethyl cellulose and HPMC in an amount needed to provide a specific unit dosage administered once-a-day to provide a therapeutic blood plasma level of venlafaxine over the entire 24-hour period of administration.

"with diminished incidence(s) of nausea and emesis" - a decrease in the number of patients suffering from nausea and vomiting compared to patients receiving the same total daily dose of an immediate release formulation that is administered at least twice a day.

[68] Spilker Decl. ¶ 20.

"for eliminating the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of venlafaxine hydrochloride" - the peak(s) and trough(s) due to the "therapeutic metabolism" of any second or third dose given in a single day is eliminated by dosing only once every 24 hours.

Dated: May 8, 2007

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CERTIFICATE OF SERVICE

I hereby certify that on this 15th day of May, 2007, I electronically filed the foregoing document, **REDACTED VERSION OF DEFENDANT IMPAX LABORATORIES, INC.'S OPENING CLAIM CONSTRUCTION BRIEF,** with the Clerk of the Court using CM/ECF which sent notification of such filing to the following:

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